

## REMARKS

This application has been reviewed in light of the Office Action dated June 17, 2003. Claims 1 to 26 are in the application, of which Claims 1 and 20 are independent. Claim 8 has been amended. Reconsideration and further examination are respectfully requested.

Claim 8 was rejected under 35 U.S.C. § 112, second paragraph, for alleged indefiniteness. In response, Claim 8 has been amended so as to clarify that step (1-4) is the removal of the solvent from the hybrid (C) and the fluorescent dye (D) between steps (1) and (2). In response to the Examiner's inquiry as to whether or not the gas flow in Claim 8 is used to dry the hybrid (C) and the fluorescent dye (D) on the substrate, the Examiner is respectfully referred to pages 11 and 12 in the specification and to Claims 1 and 8. Claim 8 clearly states that the solvent is removed between steps (1) and (2) and does not mention that the removal of the solvent is for drying. Instead, according to Claim 1, step (2) is for drying. The foregoing is also explained in the specification on pages 11 and 12. Accordingly, withdrawal of the § 112 rejection is respectfully requested.

Claims 1 to 7, 9, 11 to 15, 18, 20 to 22 and 25 were rejected under 35 U.S.C. § 103(a) over WO 87/06956 (Sutherland) in view of U.S. Patent No. 6,277,628 (Johann). Claim 10 was rejected under 35 U.S.C. § 103(a) over Sutherland in view of Johann, and further in view of JP 404330300 (Miyakoshi). Claims 16, 17, 19, 23, 24 and 26 were rejected under 35 U.S.C. § 103(a) over Sutherland in view of Johann, and further in view of "Nucleic Acid Research", 1995, Vol. 23(8), pp. 1445 to 1446 (Yamamoto). The rejections are respectfully traversed.

The presently claimed invention, as defined in Claims 1 and 20, is directed to a method of dry detection/quantification of target nucleotide chains, in which a probe and target

nucleotide chain are hybridized to form a hybrid in a solution, fluorescent dye which is capable of fluorescence in a dried state is added to the hybrid, the hybrid and fluorescent dye are dried on a substrate, and fluorescence of the dried product is measured. One difference between the methods of Claims 1 and 20 is explained on page 11 of the specification. In Claim 1, when hybridization is carried out, the probe and target nucleotide chain are fixed on a substrate in the solution. In Claim 20, on the other hand, when hybridization is carried out, the probe and target nucleotide chain are dissolved in the solution.

As Applicants understand the applied art, none of it, alone or in combination, discloses or suggests the foregoing method.

Although Sutherland may be deemed to teach the combining of fluorescent dye and a hybrid, as stated in the Office Action, Sutherland is not seen to disclose the step of drying the hybrid and the fluorescent dye on the substrate. In addition, Sutherland is not seen to disclose or teach the use of a fluorescent dye that emits fluorescence even after it is dry.

Meanwhile, Johann is said to teach the drying of biomolecular probes and fluorescent dyes and detection of the fluorescent dye after drying.

The Office Action asserted that one of ordinary skill in the art would have been motivated to apply the drying step of Johann to the method of Sutherland in light of Johann's alleged increases in hybridization throughput with small samples. Applicants disagree. Regardless of other teachings of Johann, it basically describes a dry system, such that it would be illogical to make a combination with the in-solution system of Sutherland.

Specifically as repeatedly emphasized by Sutherland, Sutherland's focus is detecting probe and nucleotide hybrids in a solution. As Applicants understand Sutherland, its

primary concern was the ability to make accurate measurements of the hybrids while in a solution, without otherwise disturbing or altering the solution. Sutherland makes no mention of detection of hybrids out of a solution or detection while the hybrids and fluorescent dye are dry.

Thus, the attempted combination of Sutherland's in-solution system with Johann's dried system could destroy the basic operating principles of Sutherland, rendering it unsatisfactory for its intended purposes. See MPEP § 2143.01. As such, the proposed combination would not have commended itself to those of ordinary skill in the art.

Furthermore, as explained on page 5, one aim of Sutherland is to avoid the need for skilled manipulations of the hybrids. However, the step of drying the hybrids and fluorescent dye involves an extra manipulation of the hybrids. Therefore, one of ordinary skill in the art would not have been motivated to apply the drying step of Johann to Sutherland because Sutherland teaches away from the use of extra manipulations.


Miyakoshi and Yamamoto have been reviewed, but are not seen to remedy the above-noted deficiencies of Sutherland.

In view of the foregoing, withdrawal of the § 103 rejections are respectfully requested.

No other matters being raised, it is believed the entire application is fully in condition for allowance, and such action is courteously solicited.

Applicants' undersigned attorney may be reached in our Costa Mesa, California office at (714) 540-8700. All correspondence should continue to be directed to our below-listed address.

Respectfully submitted,

  
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Attorney for Applicants  
Registration No. 54,334

FITZPATRICK, CELLA, HARPER & SCINTO  
30 Rockefeller Plaza  
New York, New York 10112-2200  
Facsimile: (212) 218-2200

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